

REMARKS

I. STATUS OF THE CLAIMS

Upon entry of this amendment, claims 56-59, 61, and 64-68 are pending in this application and are presented for examination. Claim 58 has been withdrawn. Claims 60 and 62-63 have been canceled without prejudice to future prosecution. Claims 56, 61, and 65-67 have been amended.

Support for the amendments to the claims is found throughout the specification as filed. In particular, support is found, for example, on page 5, lines 28-30; on page 6, lines 21-25; from page 35, line 13 to page 36, line 4; on page 36, lines 11-14; on page 75, lines 4-9; from page 76, line 27 to page 77, line 4; on page 93, lines 9-23; in Table 1 on page 93 (GRO1); and in Table 1 on page 100 (SLC26A2) of the instant specification.

Applicant has also amended claim 56 to add appropriate sequence identifiers into the claim. In addition, Applicant has amended claims 61 and 65-67 to establish proper claim dependency and/or proper antecedent basis for the term "nucleic acid probes."

As such, no new matter has been introduced. Accordingly, Applicant respectfully requests that the amendments to the claims be entered.

II. REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 56-57, 59, and 64-68 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking sufficient written description. To the extent the rejection applies to the amended claims, Applicant respectfully traverses the rejection.

In making the present rejection, the Examiner acknowledges that the Federal Circuit has stated that adequate written description is present for a genus of nucleic acids based on their hybridization properties "if they hybridize under highly stringent conditions to known sequences because such conditions dictate that all species within the genus will be structurally similar." *See*, Office Action at page 7, *quoting Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1327, 63 USPQ2d 1602, 1615 (Fed. Cir. 2002). However, the Examiner alleges that Applicant has failed to claim probes that hybridize under "stringent" conditions. *See, id.*

In an earnest effort to expedite prosecution and without acquiescing on the merits of the rejection, Applicant has amended claim 56 to clarify that the nucleic acid probes hybridize under **high stringency conditions** to the GRO1 or SLC26A2 gene product. As such, Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

III. REJECTION UNDER 35 U.S.C. § 102(b)

Claims 56-57, 59, and 64-68 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Heller *et al.* (*Proc. Natl. Acad. Sci. USA*, 94:2150-2155 (1997)). To the extent the rejection applies to the amended claims, Applicant respectfully traverses the rejection.

The Examiner alleges that Heller *et al.* teaches using a microarray to detect the expression of various genes including GRO1. *See*, Office Action at page 9. In response, Applicant asserts that Heller *et al.* fails to teach or suggest all of the elements of the claimed invention.

In an earnest effort to expedite prosecution and without acquiescing on the merits of the rejection, Applicant has amended claim 56 to recite that the presently claimed array comprises nucleic acid probes for determining an expression level of **both** GRO1 **and** SLC26A2 gene products. Applicant asserts that Heller *et al.* discloses the differential expression of genes from rheumatoid arthritis and IBD samples that do **not** correspond to the claimed combination of genes.

The Examiner further states that “[a] recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.” *See*, Office Action at page 9. According to the Examiner, Heller *et al.* teaches that a microarray containing probes for the GRO1 gene can be used to monitor GRO1 expression levels, thus demonstrating that the microarray is capable of performing the intended use of the claimed invention. *See*, Office Action at page 10.

In response, Applicant submits that the microarray taught by Heller *et al.* is clearly **not** capable of performing the intended use of the presently claimed array because it does

not contain probes for determining **both** GRO1 and SLC26A2 gene expression levels. As such, the microarray of Heller *et al.* cannot be used to monitor SLC26A2 expression levels to indicate that a subject has UC when SLC26A2 expression levels are decreased relative to normal tissue.

For the foregoing reasons, Applicant asserts that Heller *et al.* does not anticipate the presently claimed array because each and every element as set forth in amended claim 56 is not found in the reference. Accordingly, Applicant respectfully requests that the Examiner withdraw the rejection under 35 U.S.C. § 102(b).

IV. REJECTIONS UNDER 35 U.S.C. § 103(a)

A claim is considered obvious “if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.” 35 U.S.C. § 103(a). The Supreme Court in *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1395-97 (2007), identified a number of rationales to support a conclusion of obviousness which are consistent with the proper “functional approach” to the determination of obviousness as laid down in *Graham*. The key to supporting any rejection under 35 U.S.C. § 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in *KSR* noted that the analysis supporting a rejection under 35 U.S.C. § 103 should be made explicit. One of the rationales addressed by the court in *KSR* supports a finding of obviousness when the prior art reference (or combination of references): (1) teaches or suggests the claim elements; (2) provides some suggestion or motivation to combine the references; and (3) provides a reasonable expectation of success. M.P.E.P. § 2143.

A. Heller et al. in view of Lockhart et al.

Claims 56-57, 59-61, and 64-68 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Heller *et al.* in view of Lockhart *et al.* (*Nat. Biotech.*, 14:1675-1680 (1996)). To the extent the rejection applies to the amended claims, Applicant respectfully traverses the rejection.

The Examiner alleges that one of skill in the art would have been motivated to design a microarray comprising short oligonucleotide probes for the GRO1 gene based on the teachings of Heller *et al.* and Lockhart *et al.* See, Office Action at page 11. In response, Applicant asserts that the presently claimed invention is not obvious in view of the cited art for at least the following reason: the combination of references does not teach or suggest all the elements of the presently claimed invention.

As discussed above, Heller *et al.* does not teach or suggest the presently claimed array comprising nucleic acid probes of 12-40 nucleotides in length for determining an expression level of **both** GRO1 and SLC26A2 gene products. Rather, this reference discloses the differential expression of genes from rheumatoid arthritis and IBD samples that do not correspond to the claimed combination of genes. In fact, the Examiner has acknowledged that Heller *et al.* does not explicitly teach the use of short oligonucleotide probes as presently claimed. See, Office Action at page 11.

The secondary reference cited by the Examiner fails to supply the teaching that is clearly lacking in Heller *et al.* In particular, Applicant asserts that Lockhart *et al.* is completely silent regarding the presently claimed array of nucleic acid probes for determining **both** GRO1 and SLC26A2 gene expression levels.

Since neither of the references cited by the Examiner contemplates the presently claimed invention, it necessarily follows that the **combination** of these references fails to disclose or suggest all of the elements of the presently claimed invention. Importantly, these references, even when **combined**, lack any teaching or suggestion whatsoever regarding the claimed array of nucleic acid probes for determining **both** GRO1 and SLC26A2 gene expression levels. As such, Applicant asserts that there is simply no rational underpinning to combine the cited references to support a legal conclusion of obviousness because these references, whether alone or in combination, fail to teach or suggest all the elements of the claimed invention.

Accordingly, Applicant respectfully requests that the Examiner withdraw the present rejection under 35 U.S.C. § 103(a).

B. Cocks et al. in view of Heller et al.

Claims 56-57, 59, and 64-68 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Cocks et al. (U.S. Patent No. 6,607,879) in view of Heller et al. To the extent the rejection applies to the amended claims, Applicant respectfully traverses the rejection.

The Examiner alleges that one of skill in the art would have been motivated to design a microarray comprising probes for the GRO1 gene based on the teachings of Cocks et al. and Heller et al. See, Office Action at page 14. In response, Applicant asserts that the presently claimed invention is not obvious in view of the cited art for at least the following reason: the combination of references does not teach or suggest all the elements of the presently claimed invention.

Applicant submits that Cocks et al. does not teach or suggest the presently claimed array comprising nucleic acid probes of **12-40 nucleotides** in length for determining an expression level of **both** GRO1 and SLC26A2 gene products. Rather, this reference discloses cDNA probes instead of short oligonucleotide probes (i.e., 12-40 nucleotides in length). In addition, this reference discloses the differential expression of genes that do not include the claimed combination of genes. In fact, the Examiner has acknowledged that Cocks et al. does not explicitly teach a microarray comprising probes for the GRO1 gene. See, Office Action at page 13.

The secondary reference cited by the Examiner fails to supply the teaching that is clearly lacking in Cocks et al. In particular, Applicant asserts that Heller et al. is completely silent regarding the presently claimed array of nucleic acid probes having **12-40 nucleotides** for determining **both** GRO1 and SLC26A2 gene expression levels.

Since neither of the references cited by the Examiner contemplates the presently claimed invention, it necessarily follows that the **combination** of these references fails to disclose or suggest all of the elements of the presently claimed invention. Importantly, these references, even when **combined**, lack any teaching or suggestion whatsoever regarding the claimed array of nucleic acid probes having **12-40 nucleotides** for determining **both** GRO1 and SLC26A2 gene expression levels. As such, Applicant asserts that there is simply no rational underpinning to combine the cited references to support a legal conclusion of obviousness

because these references, whether alone or in combination, fail to teach or suggest all the elements of the claimed invention.

In view of the foregoing, Applicant respectfully requests that the Examiner withdraw the present rejection under 35 U.S.C. § 103(a).

C. Dieckgraefe et al. in view of Heller et al.

Claims 56-57, 59-61, and 64-68 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Dieckgraefe et al. (*Gastroenterology*, 114:A964-965 (1998)) in view of Heller et al. To the extent the rejection applies to the amended claims, Applicant respectfully traverses the rejection.

The Examiner alleges that one of skill in the art would have been motivated to design a microarray comprising probes for the GRO1 gene based on the teachings of Dieckgraefe et al. and Heller et al. See, Office Action at page 16. In response, Applicant asserts that the presently claimed invention is not obvious in view of the cited art for at least the following reason: the combination of references does not teach or suggest all the elements of the presently claimed invention.

Applicant submits that Dieckgraefe et al. does not teach or suggest the presently claimed array comprising nucleic acid probes of 12-40 nucleotides in length for determining an expression level of **both** GRO1 and SLC26A2 gene products. Rather, Dieckgraefe et al. discloses an array that detected changes in the expression of different classes of genes in IBD specimens, but without reference to any particular genes in those classes. As a result, this reference fails to teach or suggest the presently claimed array in which the expression levels of the claimed combination of genes are determined. In fact, the Examiner has acknowledged that Dieckgraefe et al. does not specifically teach probes for the GRO1 gene. See, Office Action at page 15.

The secondary reference cited by the Examiner fails to supply the teaching that is clearly lacking in Dieckgraefe et al. As discussed above, Heller et al. is completely silent regarding the presently claimed array of nucleic acid probes for determining **both** GRO1 and SLC26A2 gene expression levels.

Since neither of the references cited by the Examiner contemplates the presently claimed invention, it necessarily follows that the **combination** of these references fails to disclose or suggest all of the elements of the presently claimed invention. Importantly, these references, even when **combined**, lack any teaching or suggestion whatsoever regarding the claimed array of nucleic acid probes for determining **both** GRO1 **and** SLC26A2 gene expression levels. As such, Applicant asserts that there is simply no rational underpinning to combine the cited references to support a legal conclusion of obviousness because these references, whether alone or in combination, fail to teach or suggest all the elements of the claimed invention.

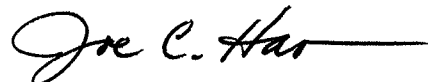
Accordingly, Applicant respectfully requests that the Examiner withdraw the present rejection under 35 U.S.C. § 103(a).

CONCLUSION

In view of the foregoing, Applicant believes all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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